## REMARKS

Consideration of the captioned application in view of the foregoing amendments and following remarks is requested.

Claims 1-4, 6, 8, 10-29, and 31-37 are currently pending. Claims 5, 7, 9, and 30 are hereby cancelled, and claims 1, 8, 12, 13, 17, 19, 20, 22, 23, 25, and 29 are hereby amended, without disclaimer of or prejudice to the subject matter deleted therein.

It is noted with appreciation that the Patent Office indicated that claims 4, 16, 24, 25, and 28 are allowable.

Claim 1 was amended to limit $R^2$ to be H and to delete C-2 and C-4 (and the proviso is no longer required based on this amendment) in view of the art based rejections. Claims 8, 17, 20, and 23 where amended to recite, *inter alia*, the treatment of breast cancer, based on the Patent Office's comments at pages 3 and 4 of the Office Action. Support for the amendment is found in throughout the Specification, at for example, page 24, line 35, and the claims as originally filed. Compounds of Formula I in claims 8 and 12 have been replaced with reference to compounds of claim 1. The term "or" has been added to claim 13 as suggested by the Patent Office. Typographical errors have been corrected in claims 22 and 25 in the term "according". Claim 29 has been changed to be direct to a "compound" instead of a "product". Claims 31-38 are newly added. Support for the amendments is found in throughout the Specification at, for example, page 11, lines 11 and 17-18. Any subject matter deleted from the pending claims may be re-introduced in this or any other patent application claiming the benefit of priority to this patent application.

**Claim Objection**

Claim 30 was objected to under 37 CFR 1.17(c) as being of improper dependent form. (Office Action at page 3.) Claim 30 has been cancelled without prejudice. The objection is now moot and withdrawal thereof is respectfully requested.

**Indefiniteness Rejection**

Claims 8, 17, 20, and 23 were rejected under 35 USC §112, second paragraph. (Office Action at page 2.) In making the rejection, the Patent Office asserted that "[d]efining a disease(s) by its (their) underlying cause renders the scope of intended uses indeterminate." (*Id.*)

For the reasons set forth below, the rejection is traversed.

Amended claims 8, 17, 20, and 23 have been amended to recite treating breast cancer. It is believed that this amendment overcomes the instant rejection and withdrawal thereof is respectfully requested.

Claim 13 was rejected under 35 USC §112, second paragraph. (Office Action at page 2.) In making the rejection, the Patent Office asserted that "the recited in claim 13 should be recited as alternate routes and that an 'or' could be added". (*Id.*)

For the reasons set forth below, the rejection is traversed.

The term "or" has been added in claim 13 in an attempt to overcome this rejection. It is believed that the rejection is now moot and withdrawal thereof is respectfully requested.

Claims 29 were rejected under 35 USC §112, second paragraph. (Office Action at page 2.) In making the rejection, the Patent Office asserted that "[t]he 'product' recited in claim 29 requires clarification." (*Id.*)

For the reasons set forth below, the rejection is traversed.

Amended claim 29 recites term "compound" instead of the term "product." It is believed that the instant rejection has been overcome and withdrawal thereof is respectfully requested."

**Enablement Rejection**

Claims 8, 17, 20, and 23 were rejected under 35 USC §112, first paragraph, on the asserted grounds that "the claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." (Office Action at page 3.) The Patent Office admitted, however, that the specification enables claims 10, 11, 18, 19, 21, 22, 24, and 25. (*Id.*) The Patent Office admitted that PARP inhibitors are known to treat breast cancer. (Office Action at pages 3-4.)

For the reasons set forth below, the rejection is traversed.

Claims 8, 17, 20, and 23 have been amended to recite treating breast cancer. It is believed that this amendment overcomes the instant rejection and withdrawal thereof is respectfully requested.

**Anticipation Rejection**

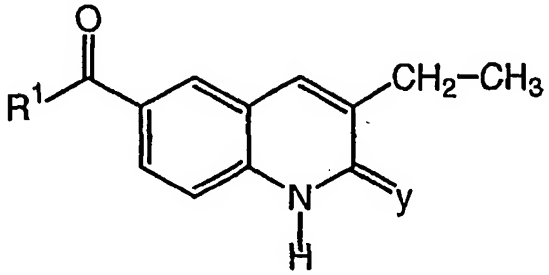
Claims 1, 6, 8, 13, 29, and 30 were rejected under 35 USC §102(b) as anticipated by WO 02/28837 ("Mabire").

For the reasons set forth below, the rejection respectfully is traversed.

Mabire discloses

Due to their mGluR antagonistic activity, more in particular their Group I mGluR antagonistic activity and even more in particular, their mGluR1 antagonistic activity, the compounds of formula (I-A) or (I-B), their *N*-oxides, pharmaceutically acceptable addition salts, quaternary amines and stereochemically isomeric forms are useful in the treatment or prevention of glutamate-induced diseases of the central nervous sytem. Diseases in which a role for glutamate has been demonstrated include drug addiction abstinence (dependence, opioid tolerance, opioid withdrawal), hypoxic, anoxic and ischemic injuries (ischemic stroke, cardiac arrest), pain (neuropathic pain, inflammatory pain, hyperalgesia), hypoglycemia, diseases related to neuronal damage, brain trauma head trauma, spinal cord injury, myelopathy, dementia, anxiety, schizophrenia, depression, impaired cognition, amnesia, bipolar disorders, conduct disorders, Alzheimer's disease, vascular dementia, mixed (Alzheimer's and vascular) dementia, Lewy Body disease, delirium or confusion, Parkinson's disease, Huntington's disease Down syndrome, epilepsy, aging, Amyotrophic Lateral Sclerosis, multiple sclerosis, AIDS (Acquired Immune Deficiency Syndrome) and AIDS related complex (ARC). (Mabire at page 26.)

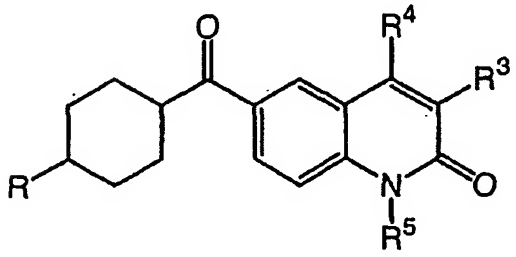
Table 3



(Mabire at page 78)

| Co. no. | Ex. no. | Y. | $R^1$ | physical data |
|---|---|---|---|---|
| 146 | B4 | O | 4-(dimethylethyl)cyclohexyl | mp. 230°C |
| 148 | B4 | O | 4-methylcyclohexyl | trans; mp. 214°C |

Table 4



( Mabire at page 80)

| Co. no. | Ex. no. | $R^3$ | $R^4$ | $R^5$ | R | physical data |
|---|---|---|---|---|---|---|
| 50 | B7 | methyl | H | H | H | mp. 256.1°C |

In making the rejection, the Patent Office stated that Mabire "describes several compounds within the claims' scope for uses including those embraced herein. (Office Action at page 5.)

As is well settled, anticipation requires "identity of invention." Each and every element recited in a claim must be found in a single prior art reference and arranged as in the claim.

Amended claim 1 no longer provides that $R^2$ together with $R^3$ may form =O. It is believed that in view of this amendment, the instant rejection is moot and should be withdrawn.

Claim 8 was rejected under 35 USC §102(b) as anticipated by EP 0 371 564 ("Freyne").

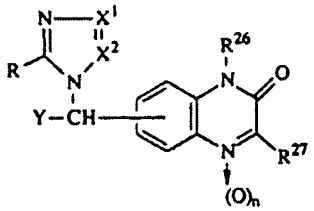
For the reasons set forth below, the rejection respectfully is traversed.

Freyne discloses

> In view of their capability to delay the metabolism of retinoic acid the compounds can thus be used in the treatment of disorders which are characterized by an increased proliferation and/or abnormal differentiation of epithelial cells. In particular the compounds of the invention can be used for treatment of carcinoma which is essentially a derailment of cellular differentiation, occurring in epithelial tissues. Other uses include, in addition to cancer treatment, the treatment of a variety of disorders of keratinization such as, for example, acne, psoriasis, lamellar ichthyosis, plantar warts, callosites, acanthosis nigricans, lechen planus, molluscum, melasma, corneal epithelial abrasion, geograpic tongue, Fox-Fordyce disease, cutaneous mestatic melanoma and heloids, epidermolytic hyperkeratosis, Darier's disease, pityriasis rubra pilaris, congenital ichthyosiform erythroderma, hyperkeratosis palmaris et plantaris, and similar diseases.

(Freyne at page 31)

Table 9-c



| Comp. No. | Ex. No. | R | -X¹=X²- | Y | p | R26 | R27 | n | mp.(°C) / base / salt |
|---|---|---|---|---|---|---|---|---|---|
| 126-c | 20-c | H- | -CH=CH- | c.$C_6H_{11}$- | 6 | H- | $CH_3$- | 0 | 174.8 |

(Freyne at page 78-80.)

In making the rejection, the Patent Office admitted that "claim 1 excludes the species (126-c) in Freyne, [but] claim 8 does not." (Office Action at page 5.)

Claim 8 has been amended to be limited to the compounds included in the scope of claim 1. With this amendment, it is believed that the rejection is moot and should be withdrawn.

**Obviousness Rejection**

Claims 1, 6, 13, 29, and 30 were rejected under 35 USC §103(a) as being unpatentable over Freyne. (Office Action at page 6.)

For the reasons set forth below the rejection, respectfully is traversed.

Freyne's disclosure set forth above is incorporating herein by reference.

In making the rejection, the Patent Office acknowledged, however, that Species 126-C in Freyne is not encompassed by the claims of the captioned application. (Office Action at page 6.)

To fill the acknowledged gap, the Patent Office relied upon the assertion that the closest claimed compounds "are simply higher homologs at the 3-position or are substituted with other azoles included within the definition of Z." (Office Action at page 6.) The Patent Office also stated that claim 13 was rejected "since Freyne uses the same processes as route b) to make imidazole species, 126-c. (*Id.*)

The Patent Office then concluded that "it would have been obvious to one skilled in the art at the time the instant invention was made to modify 126-c of Freyne by inserting higher alkyls at the 3-position and/or replacing the imidazole ring with triazoles with the expectation that such resulting compounds will also have the uses reported in Freyne in view of the equivalence teachings." (*Id.*)

Claim 1 has been amended to remove c-2 and c-4 from the definition of Z. With this amendment it is believed that the instant rejection has been overcome and withdrawal thereof is respectfully requested.

Claim 12 was rejected under 35 USC §103(a) as being unpatentable over Freyne as applied to claims 1, 6, 13, 29, and 30 above, and further in view of US 2003/0130505 ("Zhi"). (Office Action at page 6.)

In making the rejection, the Patent Office acknowledged, however, that Species 126-C in Freyne is not encompassed by the claims of the captioned application and that no particular disclosure of adding chemotherapeutic agents is found. (Office Action at page 6.)

To fill the acknowledged gap, the Patent Office relied upon Zhi to "show that compounds having the same type of activity as Freyne are conventionally mixed with other active ingredients, including chemotherapeutic agents." (Office Action at pages 6-7.)

The Patent Office then concluded that "it would have been obvious to one skilled in the art at the time the instant invention was the art at the time the instant invention was made to

combine compounds such as 126-c of Freyne included in the instant scope with known anticancer agents." (Office Action at pages 6-7.)

Claim 12 has been amended to include the compounds of claim 1. In view of the amendments to claim 1 it is not believed that compounds of claim 1 are disclosed or suggested by Freyne for the reasons set forth above. Zhi does not close this gap. Therefore it is believed that the instant rejection is improper and should be withdrawn.

Finally, the Examiner is invited to call the applicants' undersigned representative if any further action will expedite the prosecution of the application or if the Examiner has any suggestions or questions concerning the application or the present Response. In fact, if the claims of the application are not believed to be in full condition for allowance, for any reason, the applicants respectfully request the constructive assistance and suggestions of the Examiner in drafting one or more acceptable claims pursuant to MPEP § 707.07(j) or in making constructive suggestions pursuant to MPEP § 706.03 so that the application can be placed in allowable condition as soon as possible and without the need for further proceedings.

Accordingly, entry of the claims and allowance of the claims is respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

Respectfully submitted,

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